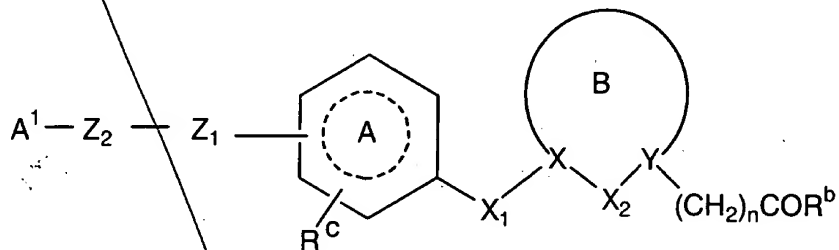
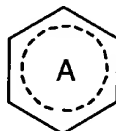


What is claimed is:

1. A compound of the formula

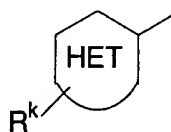


or a pharmaceutically acceptable salt thereof, wherein



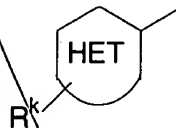
10 is a 4-8 membered monocyclic ring or 7-12 membered bicyclic ring; which ring is optionally saturated or unsaturated, which ring is optionally substituted with one or more substituent selected from the group consisting of alkyl, haloalkyl, aryl, heteroaryl, halogen, alkoxyalkyl, aminoalkyl, hydroxy, nitro, alkoxy, hydroxyalkyl, thioalkyl, amino, alkylamino, arylamino, alkylsulfonamide, acyl, acylamino, alkylsulfone, sulfonamide, allyl, alkenyl, methylenedioxy, ethylenedioxy, alkynyl, carboxamide, cyano, and $-(CH_2)_n COR$ wherein n is 0-2 and R is hydroxy, alkoxy, alkyl or amino;

15 A^1 is a 5-9 membered monocyclic or 7-14 membered polycyclic heterocycle of the formula

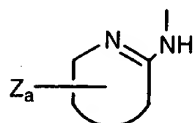


25 containing at least one nitrogen atom and optionally 1 to 4 heteroatoms or groups, selected from O, N, S, SO_2 or CO; optionally saturated or unsaturated; optionally substituted by one or more R^k selected from the group consisting of hydroxy, alkyl, alkoxy, alkoxyalkyl, thioalkyl, haloalkyl, cyano, amino, alkylamino, halogen,

acylamino, sulfonamide and -COR wherein R is hydroxy, alkoxy, alkyl or amino;

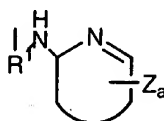


include the following heterocyclic ring systems containing at least one nitrogen atom:



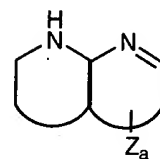
B2

or



B3

or



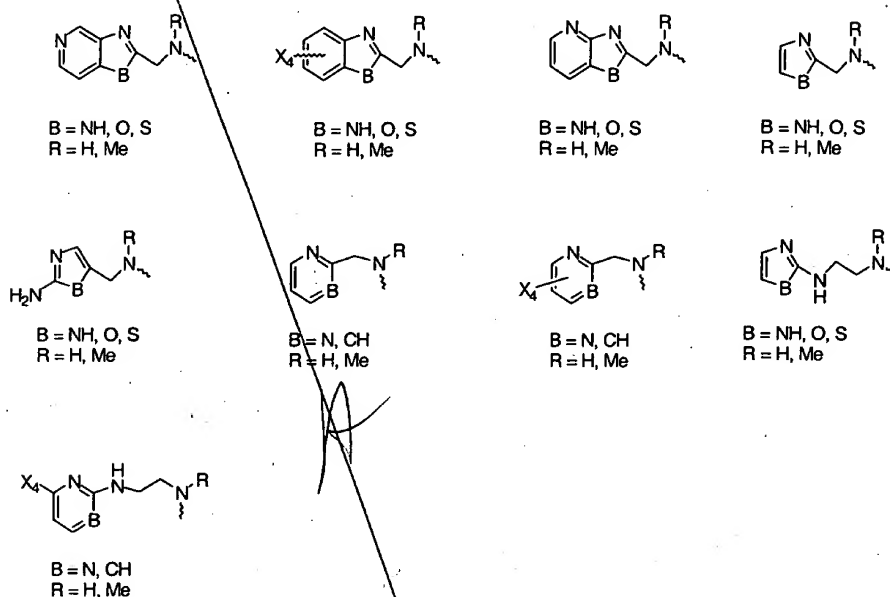
B4

wherein Z_a is H, alkyl, alkoxy, hydroxy, amine, alkylamine, dialkylamine, carboxyl, alkoxycarbonyl, hydroxyalkyl, halogen or haloalkyl and R¹ is H, alkyl, alkoxyalkyl, acyl, haloalkyl or alkoxycarbonyl, pyridylamino, imidazolylamino, morpholinopyridine, tetrahydronaphthyrine, oxazolylamino, thiazolylamino, pyrimidinylamino, quinoline, isoquinoline, tetrahydroquinoline, imidazopyridine, benzimidazole, pyridone or quinolone;

The following heteroaryls include the ring systems described above;

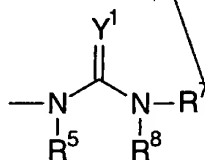
5

when Z_1 of Formula I is CO or SO_2 , the linkage A^1-Z_2 of Formula I includes the heterocycle derived ring systems: pyridine, imidazole, thiazole, oxazole, benzimidazole, imidazopyridine and heterocycles for A^1-Z_2 include :



wherein X_4 is as defined above.

10 or A^1 is



wherein Y^1 is selected from the group consisting of $N-R^2$, O, and S;

15

R^2 is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxy carbonyl; aryloxy carbonyl; haloalkylcarbonyl; haloalkoxy carbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxy carbonyl;

wherein Y^2 is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles;

Z_1 is selected from the group consisting of CH_2 , CH_2O , O, N, CO, S,

5 SO, SO_2 , $\begin{array}{c} OH \\ | \\ CH \end{array}$ and NR_k wherein R_k is selected from H or lower alkyl;

Z_2 is a 1-5 carbon linker optionally containing one or more heteroatom selected from the group consisting of O, S and N; alternatively $Z_1 - Z_2$ may further contain a carboxamide, sulfone, 10 sulfonamide, alkenylene, alkynylene, or acyl group;

wherein the carbon and nitrogen atoms of $Z_1 - Z_2$ are optionally substituted by alkyl, alkoxy, thioalkyl, alkylsulfone, aryl, alkoxyalkyl, hydroxy, alkylamino, heteroaryl, alkenyl, alkynyl, carboxyalkyl, 15 halogen, haloalkyl or acylamino;



wherein $Z_2 - Z_1$ is attached to at the para or meta position relative to the X_1 substituent;

n is an integer 1 or 2;

20

R^c is selected from the group consisting of hydrogen; alkyl; halogen; hydroxy, nitro, alkoxy, amino, haloalkyl, aryl, heteroaryl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, thioalkyl, alkylamino, arylamino, alkylsulfonylamino, acyl, acylamino, sulfonyl, sulfonamide, allyl, 25 alkenyl, methylenedioxy, ethylenedioxy, alkynyl, alkynylalkyl, carboxy, alkoxycarbonyl, carboxamido, cyano, and $-(CH_2)_n COR$ wherein n is 0-2 and R is selected from hydroxy, alkoxy, alkyl and amino;

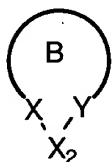
X₁ is selected from the group consisting of -O-, CO, SO₂, NR^m and (CHR^p)_q; wherein R^m is H or alkyl; R^p is H, alkyl; alkoxy or hydroxy; q is 0 or 1;

5 X₂ is selected from the group consisting of -CHR^e-, CO, SO₂, O, NR^f and S; wherein R^f is H or alkyl;

R^e is selected from the group consisting of H, alkyl, hydroxy and alkoxy;

10 X or Y are independently selected from the group consisting of -CR^g- or -N- wherein R^g is selected from the group consisting of H, alkyl, haloalkyl, fluoro, alkoxyalkyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkylsulfone, hydroxyalkyl, hydroxy, alkoxy, and carboxyalkyl;

15 optionally the group X-X₂-Y contains a moiety selected from the group consisting of acyl, alkyl, amino, ether, thioether, sulfone and olefin;



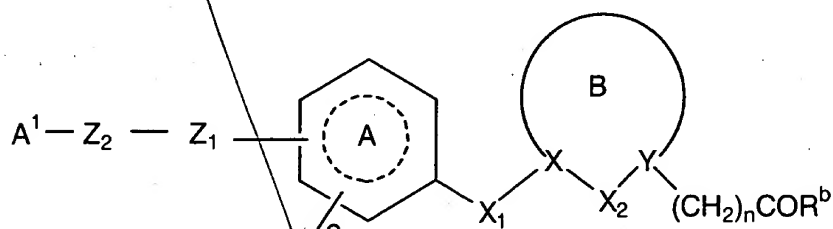
20 forms a 3-8 membered monocyclic ring system; or an 8-11 membered bicyclic system; optionally saturated or unsaturated; the monocyclic ring system optionally containing 1-2 heteroatoms selected from N, O and S; the bicyclic ring system optionally containing 1-4 heteroatoms selected from N, O and S, or optionally containing the group such as SO₂ or CO; and optionally substituted with one or more substituent selected from the group consisting of alkyl, halogen, cyano, carboalkoxy, haloalkyl, alkoxyalkyl, alkylsulfone, aryl, heteroaryl, arakyl, heteroaralkyl, or alkoxy;

25

R^b is $X_3 - R^h$ wherein X_3 is selected from the group consisting of O, S and NR^i wherein R^h and R^i are independently selected from the group consisting of H, alkyl, acyl, aryl, aralkyl and alkoxyalkyl; and

5 and n is 0 or 1.

2. A compound according to the claim 1,



10 wherein

A^1 , Z_1 , Z_2 , R^b , R^c , are as described in claim 1;

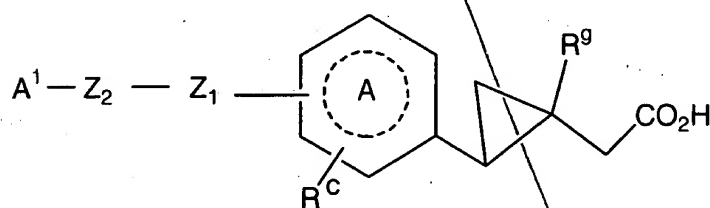
X_1 is $(CHR^p)_q$; wherein $q = 0$;

B is a 3-, 4-, or a 5-membered ring obtained by combining $X-X_2-Y$;

A is a phenyl ring substituted with R^c ;

15 $n = 1$.

3. A compound according to the claim 2,



20 wherein the ring B is a 3-member cyclopropyl ring;

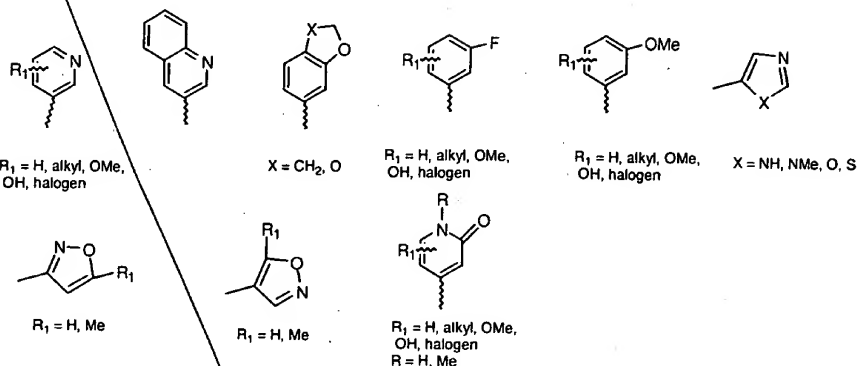
$Y = CR^g$;

wherein R^g is selected from the group consisting of H, alkyl, haloalkyl, alkoxyalkyl, alkynyl, aryl, heteroaryl, aralkyl, heteroaralkyl, alkylsulfone, hydroxyalkyl, hydroxy, alkoxy, and carboxyalkyl;

25 A is a phenyl ring substituted with R^c ;

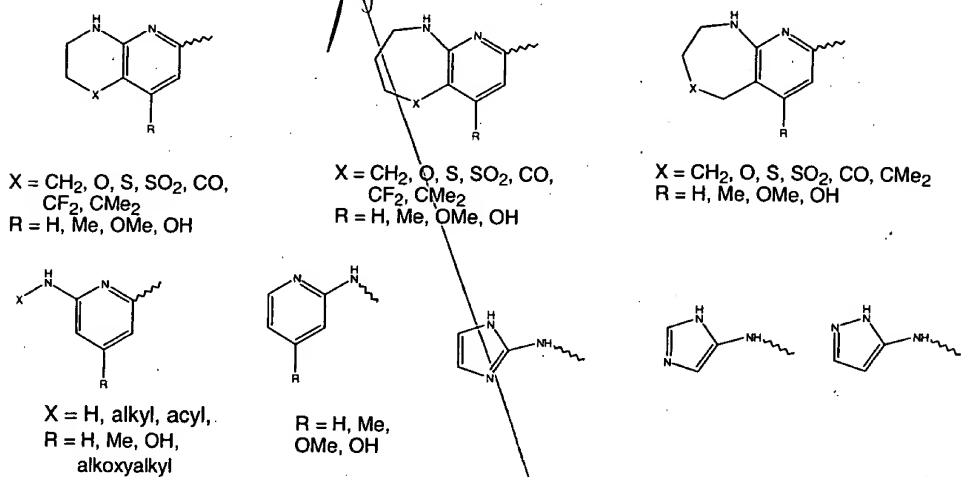
$R^b = OH$

4. A compound according to the claim 3 wherein R^9 is selected from the following substituents/groups



$\text{H, alkyl, CH}_2\text{B}_1\text{R}$ ($\text{B}_1 = \text{O, SO}_2, \text{S, CO}$; $\text{R} = \text{alkyl, aryl}$), CH_2OH , ---R $\text{R} = \text{alkyl, aryl}$
 CH_2R_1 ($\text{R}_1 = \text{aryl, heteroaryl}$)

5. A compound according to the claim 3 wherein A^1 is selected from the following ring systems



10

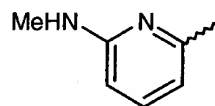
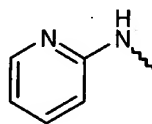
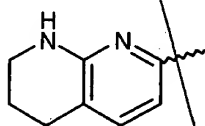
6. A compound according to the claim 3 wherein ring A is a phenyl ring, and the side chains containing $Z_1\text{-}Z_2$ and $X_1\text{-}X$ are connected para to each other.

15. 7. A compound according to the claim 6 wherein the phenyl ring is optionally substituted with one or more substituents selected from the group consisting of alkyl; halogen, hydroxy, alkoxy, haloalkyl,

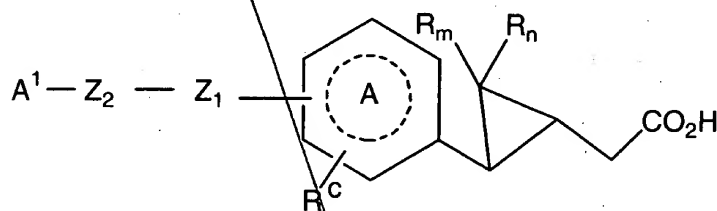
aryl, heteroaryl, alkoxyalkyl, sulfonamide, methylenedioxy, ethylenedioxy, alkynyl, and alkynylalkyl;

8. A compound according to the claim 6 wherein Z_1 is selected from the group consisting of CH_2 , CH_2O , O , NR_k , CO , S , SO , and SO_2 . R_k is as defined in claim 1

9. A compound according to the claim 6 wherein A^1 is selected from the following ring systems



10. A compound according to the claim 1,



wherein

A^1 , Z_1 , Z_2 , R^b , R^c , are as described in claim 1;

X_1 is $(CHR^p)_q$; wherein $q = 0$;

A is a phenyl ring substituted with R^c

B is a 3-member ring obtained by combining $X-X_2-Y$;

$n = 1$

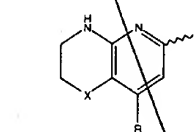
R_m and R_n are selected from the group consisting of H, alkyl,

halogen, alkoxy, haloalkyl, alkoxyalkyl, alkylsulfone, cyano,

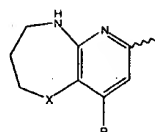
carboalkoxy, aryl, heteroaryl, aralkyl and heteroaralkyl. R_m and R_n

may form a spirocyclic ring system.

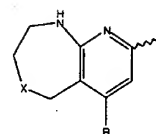
11. A compound according to the claim 10 wherein A¹ is selected from the following ring systems:



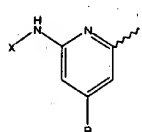
X = CH₂, O, S, SO₂, CO,
CF₂, CMe₂
R = H, Me, OMe, OH



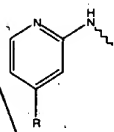
X = CH₂, O, S, SO₂, CO,
CF₂, CMe₂
R = H, Me, OMe, OH



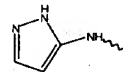
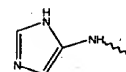
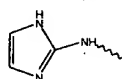
X = CH₂, O, S, SO₂, CO, CMe₂
R = H, Me, OMe, OH



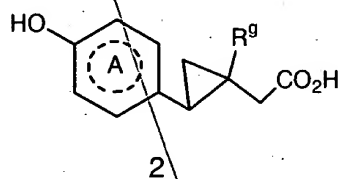
X = H, alkyl, acyl,
R = H, Me, OH,
alkoxyalkyl



R = H, Me,
OMe, OH



- 5 12. The intermediates of formula 2 for their utility in the synthesis of $\alpha\text{v}\beta 3$ and/or $\alpha\text{v}\beta 5$ integrin antagonists.



- 10 13. A compound according to Claim 1 selected from the group consisting of :

2-[4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid

2-[4-[3-(2-pyridinylamino)propoxy]phenyl] cyclopentaneacetic acid

- 15 3-[4-[3-(2-pyridinylamino)propoxy]phenyl] cyclopentaneacetic acid

2,2-difluoro-3-[4-[3(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid

(2-[4-[2-(5,6,7,8-Tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl]-cyclopropyl)-acetic acid

- 20 2-[3-methyl-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid

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T0979 99795

- 1
2-{4-[3-(1-*H*-Pyrazol-3-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- 2-{3-Fluoro-4-[3-(1-*H*-pyrazol-3-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- 5 (1-Methyl-2-{4-[2-(6-methylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (2-{4-[2-(6-Ethylamino-pyridin-2-yl)-ethoxy]-phenyl}-1-methyl-cyclopropyl)-acetic acid
- 10 [2-(4-{2-[6-(2-Methoxy-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-1-methyl-cyclopropyl]-acetic acid
- [2-(4-{2-[6-(3-Methoxy-propylamino)-pyridin-2-yl]-ethoxy}-phenyl)-1-methyl-cyclopropyl]-acetic acid
- (2-{4-[2-(6-Acetylamino-pyridin-2-yl)-ethoxy]-phenyl}-1-methyl-cyclopropyl)-acetic acid
- 15 [1-Methyl-2-(4-{2-[6-(2,2,2-trifluoro-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid
- (2-{4-[2-(6-Ethylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- 20 [2-(4-{2-[6-(2-Methoxy-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid
- [2-(4-{2-[6-(2,2,2-Trifluoro-ethylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid
- [2-(4-{2-[6-(3-Methoxy-propylamino)-pyridin-2-yl]-ethoxy}-phenyl)-cyclopropyl]-acetic acid
- 25 (2-{4-[2-(6-Acetylamino-pyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
14. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 and a pharmaceutically acceptable carrier.
- 30
15. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claims 2-13 and a pharmaceutically acceptable carrier.

- 2-[2-methoxy-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid
- 2-[2-methyl-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropane-acetic acid
- 5 2-[3-fluoro-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid
- 2-[2-fluoro-4-[3-(2-pyridinylamino)propoxy]phenyl]cyclopropaneacetic acid
- 10 2-[4-[2-[6-(methylamino)-2-pyridinyl]ethoxy]phenyl]cyclopropane-acetic acid
- 2-[4-[2-(3,4-dihydro-2*H*-pyrido[3,2-*b*]-1,4-oxazin-6-yl)ethoxy]phenyl]-cyclopropaneacetic acid
- 15 3-[4-[3-(2-pyridinylamino)propoxy]phenyl]cyclobutaneacetic acid
- (2-{2-Methoxy-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- (2-{2-Fluoro-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- (2-{2-Acetoxy-4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- 20 (1-Methyl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- (1-Methoxymethyl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- (1-Methanesulfonylmethyl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- 25 (1-Pyridin-3-yl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- (1-Benzo[1,3]dioxole-5-yl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- 30 (1-(2,3-Dihydro-benzofuran-6-yl)-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid
- (1-Isloxazol-3-yl-2-[4-[3-(pyridin-2-ylamino)-propoxy]-phenyl]-cyclopropyl)-acetic acid

- (1-Isoxazol-5-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Oxazol-5-yl-2-{4-[3-(pyridin-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- 5 (2-{4-[3-(Pyridin-2-ylamino)-propoxy]-phenyl}-1-thiazol-5-yl-cyclopropyl)-acetic acid
- (1-Methyl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Methoxymethyl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- 10 (1-Methanesulfonylmethyl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Pyridin-3-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- 15 (1-(2,3-Dihydro-benzofuran-6-yl)-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Benzo[1,3]dioxol-5-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Isoxazol-3-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- 20 (1-Isoxazol-5-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- (1-Oxazol-5-yl-2-{4-[2-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-cyclopropyl)-acetic acid
- 25 (2-{4-[2-(5,6,7,8-Tetrahydro-[1,8]naphthyridin-2-yl)-ethoxy]-phenyl}-1-thiazol-5-yl-cyclopropyl)-acetic acid
- (2-{4-[3-(1-*H*-Imidazol-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- (2-{3-Fluoro-4-[3-(1-*H*-imidazol-2-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- 30 (2-{3-Fluoro-4-[3-(3-*H*-imidazol-4-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid
- (2-{4-[3-(3-*H*-Imidazol-4-ylamino)-propoxy]-phenyl}-cyclopropyl)-acetic acid

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- 5
16. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 1 and a pharmaceutically acceptable carrier/or additive and optionally other active ingredient
- 10
17. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claims 2-15 and a pharmaceutically acceptable carrier/or additive and optionally other active ingredient
- 15
18. A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v\beta_3$ inhibiting amount of a compound of Claim 1.
- 20
19. A method for treating conditions mediated by the $\alpha_v\beta_3$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v\beta_3$ inhibiting amount of a compound of Claims 2-13.
- 25
20. The method according to Claim 16 wherein the condition treated is tumor metastasis.
- 30
21. The method according to Claim 17 wherein the condition treated is tumor metastasis.
22. The method according to Claim 16 wherein the condition treated is solid tumor growth.
23. The method according to Claim 17 wherein the condition treated is solid tumor growth.
24. The method according to Claim 16 wherein the condition treated is angiogenesis.

1. The first part of the report is a general statement of the purpose of the study.

25. The method according to Claim 17 wherein the condition treated is angiogenesis.
26. The method according to Claim 16 wherein the condition treated is osteoporosis.
27. The method according to Claim 17 wherein the condition treated is osteoporosis.
28. The method according to Claim 16 wherein the condition treated is humoral hypercalcemia of malignancy.
29. The method according to Claim 17 wherein the condition treated is humoral hypercalcemia of malignancy.
30. The method according to Claim 16 wherein the condition treated is smooth muscle cell migration.
31. The method according to Claim 17 wherein the condition treated is smooth muscle cell migration.
32. The method according to Claim 16 wherein restenosis is inhibited.
33. The method according to Claim 17 wherein restenosis is inhibited.
34. The method according to Claim 16 wherein atherosclerosis is inhibited.
35. The method according to Claim 17 wherein atherosclerosis is inhibited.
36. The method according to Claim 16 wherein macular degeneration is inhibited.

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37. The method according to Claim 17 wherein macular degeneration is inhibited.
- 5 38. The method according to Claim 16 wherein retinopathy is inhibited.
39. The method according to Claim 17 wherein retinopathy is inhibited.
40. The method according to Claim 16 wherein arthritis is inhibited.
- 10 41. The method according to Claim 17 wherein arthritis is inhibited.
42. A method for treating conditions mediated by the $\alpha_v\beta_5$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v\beta_5$ inhibiting amount of a compound of Claim 1.
- 15 43. A method for treating conditions mediated by the $\alpha_v\beta_5$ integrin in a mammal in need of such treatment comprising administering an effective $\alpha_v\beta_5$ inhibiting amount of a compound of Claim 2.
- 20 44. The method according to Claim 40 wherein the condition treated is tumor metastasis.
45. The method according to Claim 41 wherein the condition treated is tumor metastasis.
- 25 46. The method according to Claim 40 wherein the condition treated is solid tumor growth.
- 30 47. The method according to Claim 41 wherein the condition treated is solid tumor growth.

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48. The method according to Claim 40 wherein the condition treated is angiogenesis.
- 5 49. The method according to Claim 41 wherein the condition treated is angiogenesis.
50. The method according to Claim 40 wherein the condition treated is osteoporosis.
- 10 51. The method according to Claim 41 wherein the condition treated is osteoporosis.
52. The method according to Claim 40 wherein the condition treated is humoral hypercalcemia of malignancy.
- 15 53. The method according to Claim 41 wherein the condition treated is humoral hypercalcemia of malignancy.
54. The method according to Claim 40 wherein the condition treated is smooth muscle cell migration.
- 20 55. The method according to Claim 41 wherein the condition treated is smooth muscle cell migration.
- 25 56. The method according to Claim 40 wherein restenosis is inhibited.
57. The method according to Claim 41 wherein restenosis is inhibited.
58. The method according to Claim 40 wherein atherosclerosis is inhibited.
- 30 59. The method according to Claim 41 wherein atherosclerosis is inhibited.

